Supplementary Information

Discovery of a Novel Acetone Hemisolvate of Metacetamol via Swift Cooling Crystallization

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Single crystal X-ray diffraction (SCXRD) of metacetamol form I and acetone hemisolvate

Table S1. Data collection conditions and results of SCXRD analysis of metacetamol form I and acetone hemisolvate

Identification Code	Form I	Acetone hemisolvate
Chemical formula	$C_8H_9NO_2$	$C_{19}H_{24}N_2O_5$
Formula weight	151.16 g/mol	360.40 g/mol
Temperature	296(2) K	296(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal size	0.173 x 0.182 x 0.544 mm	0.365 x 0.256 x 0.125 mm
Crystal system	orthorhombic	monoclinic
Space group	P n a 2_1	P $_1$ 2_1/c $_1$
Unit cell dimensions	a = 10.505(3) Å b = 16.986(4) Å c = 4.2444(10) Å α = 90° β = 90° γ = 90°	a = 12.136(3)Å b = 9.124(2)Å c = 17.679(5)Å α = 90° β = 99.308(8)° γ = 90°
Volume	757.4(3)Å^3	1931.8(8) Å^3
Z	4	4
Density(calculated)	1.326g/cm^3	1.239 g/cm^3
Absorption coefficient	0.096 mm^{-1}	0.090 mm^{-1}
F(000)	320	768
Theta range for data collection	3.08 to 27.11°	2.52 to 28.42°
Index ranges	-13<=h<=13, -21<=k<=21, -5<=l<=5	-15<=h<=16, -11<=k<=9, -23<=l<=23
Reflections collected	41063	13390
Independent reflections	1682 [R(int) = 0.0369]	4558 [R(int) = 0.2850]
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Refinement program	SHELXL-2016/6 (Sheldrick, 2016) 2539 / 1 / 168	SHELXL-2016/6 (Sheldrick, 2016)
Goodness-of-fitonF2	1.098	0.919
Final R indices I>2σ(I)	R1 = 0.0319, wR2 = 0.0817	R1 = 0.1004, wR2 = 0.1765
R for all	R1 = 0.0380, wR2 = 0.0847	R1 = 0.3591, wR2 = 0.2678
CCDC Number	2363635	2487202

Form I (CCDC-2363635)

Table S2. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å2).

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor

	x/a	y/b	z/c	U(eq)
O2	0.75098(14)	0.75962(8)	0.5782(6)	0.0587(5)
O1	0.64043(13)	0.38819(7)	0.2974(5)	0.0583(5)
N1	0.62331(14)	0.65316(8)	0.6135(5)	0.0383(4)
C1	0.69251(17)	0.59554(10)	0.4443(5)	0.0334(4)
C7	0.65403(19)	0.72786(10)	0.6784(5)	0.0397(5)
C2	0.64002(16)	0.52054(10)	0.4438(5)	0.0365(4)
C3	0.69958(18)	0.45967(11)	0.2891(6)	0.0388(5)
C6	0.8058(2)	0.60939(11)	0.2876(6)	0.0422(5)
C4	0.81291(19)	0.47295(11)	0.1300(6)	0.0432(5)
C5	0.86424(19)	0.54734(12)	0.1337(6)	0.0461(5)
C8	0.5605(2)	0.77120(12)	0.8798(6)	0.0509(6)

Table S3. Bond lengths (Å).

O2-C7	1.228(2)	**O1-C3**	1.364(2)
O1-H1	0.82	**N1-C7**	1.338(2)
N1-C1	1.415(2)	**N1-H1A**	0.86
C1-C6	1.383(3)	**C1-C2**	1.388(2)
C7-C8	1.496(3)	**C2-C3**	1.376(3)
C2-H2	0.93	**C3-C4**	1.387(3)
C6-C5	1.384(3)	**C6-H6**	0.93
C4-C5	1.374(3)	**C4-H4**	0.93
C5-H5	0.93	**C8-H8A**	0.96
C8-H8B	0.96	**C8-H8C**	0.96

Table S4. Bond angles (°)

C3-O1-H1	109.5	**C7-N1-C1**	129.55(17)
C7-N1-H1A	115.2	**C1-N1-H1A**	115.2
C6-C1-C2	119.80(17)	**C6-C1-N1**	124.63(16)
C2-C1-N1	115.57(17)	**O2-C7-N1**	123.03(19)
O2-C7-C8	121.75(18)	**N1-C7-C8**	115.21(18)
C3-C2-C1	120.66(18)	**C3-C2-H2**	119.7
C1-C2-H2	119.7	**O1-C3-C2**	116.70(18)
O1-C3-C4	123.25(17)	**C2-C3-C4**	120.04(17)
C1-C6-C5	118.63(17)	**C1-C6-H6**	120.7
C5-C6-H6	120.7	**C5-C4-C3**	118.74(18)
C5-C4-H4	120.6	**C3-C4-H4**	120.6
C4-C5-C6	122.1(2)	**C4-C5-H5**	118.9
C6-C5-H5	118.9	**C7-C8-H8A**	109.5

C7-C8-H8B	109.5	**H8A-C8-H8B**	109.5
C7-C8-H8C	109.5	**H8A-C8-H8C**	109.5
H8B-C8-H8C	109.5		

Table S5. Torsion angles (°)

C7-N1-C1-C6	-5.6(4)	**C7-N1-C1-C2**	173.9(2)
C1-N1-C7-O2	4.1(4)	**C1-N1-C7-C8**	-176.8(2)
C6-C1-C2-C3	0.1(3)	**N1-C1-C2-C3**	-179.47(19)
C1-C2-C3-O1	-179.2(2)	**C1-C2-C3-C4**	-0.3(3)
C2-C1-C6-C5	-0.1(3)	**N1-C1-C6-C5**	179.4(2)
O1-C3-C4-C5	179.4(2)	**C2-C3-C4-C5**	0.7(3)
C3-C4-C5-C6	-0.8(4)	**C1-C6-C5-C4**	0.5(4)

Table S6. Anisotropic atomic displacement parameters (Å2).

The anisotropic atomic displacement factor exponent takes the form: -2π2[h2 a*2 U11 + ... + 2 h k a* b* U12]

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O2	0.0498(8)	0.0295(7)	0.0967(13)	-0.0162(9)	0.0072(9)	-0.0110(6)
O1	0.0396(8)	0.0255(6)	0.1099(14)	-0.0161(9)	0.0054(9)	-0.0010(6)
N1	0.0353(7)	0.0250(7)	0.0546(9)	-0.0048(7)	0.0026(8)	-0.0033(6)
C1	0.0332(9)	0.0251(8)	0.0418(9)	-0.0020(7)	-0.0054(9)	0.0001(7)
C7	0.0404(10)	0.0260(8)	0.0525(13)	-0.0052(8)	-0.0088(9)	-0.0007(7)
C2	0.0297(8)	0.0278(9)	0.0520(11)	-0.0040(8)	-0.0016(9)	-0.0004(7)
C3	0.0341(9)	0.0248(8)	0.0576(12)	-0.0053(9)	-0.0074(9)	0.0020(7)
C6	0.0427(10)	0.0291(8)	0.0548(11)	0.0014(10)	0.0023(10)	-0.0066(8)
C4	0.0403(10)	0.0343(10)	0.0551(12)	-0.0071(10)	-0.0006(11)	0.0067(8)
C5	0.0405(10)	0.0432(11)	0.0545(13)	0.0013(11)	0.0098(10)	-0.0008(8)
C8	0.0563(13)	0.0325(9)	0.0640(15)	-0.0122(9)	0.0016(11)	0.0014(8)

Table S7. Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$)

	x/a	**y/b**	**z/c**	**U(eq)**
H1	0.6865	0.3549	0.2163	0.087
H1A	0.5508	0.6379	0.6852	0.046
H2	0.5638	0.5114	0.5491	0.044
H6	0.8419	0.6594	0.2856	0.051
H4	0.8534	0.4323	0.0230	0.052
H5	0.9407	0.5563	0.0294	0.055
H8A	0.6054	0.8048	1.0236	0.076
H8B	0.5102	0.7341	0.9965	0.076
H8C	0.5058	0.8025	0.7485	0.076

Table S8. Hydrogen bond distances (Å) and angles (°)

	Donor-H	Acceptor-H	Donor-Acceptor	Angle
C6-H6···O2	0.93	2.31	2.892(2)	119.9
N1-H1A···O1	0.86	2.11	2.963(2)	170.2
O1-H1···O2	0.82	1.84	2.634(2)	161.7
O1-H1···O2	0.82	1.84	2.634(2)	161.7
N1-H1A···O1	0.86	2.11	2.963(2)	170.2
C6-H6···O2	0.93	2.31	2.892(2)	119.9

Acetone hemisolvate (CCDC number – 2487202)

Table S9. Atomic coordinates and equivalent isotropic atomic displacement parameters ($Å^2$) U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x/a	y/b	z/c	U(eq)
O2	0.6565(3)	0.9863(4)	0.6760(2)	0.0595(11)
O1	0.4020(3)	0.8481(4)	0.4467(2)	0.0702(13)
N2	0.8438(3)	0.0007(4)	0.8157(2)	0.0467(12)
O4	0.0930(4)	0.6609(4)	0.9696(2)	0.0809(14)
N1	0.4036(4)	0.6478(4)	0.5220(2)	0.0583(13)
O3	0.9074(4)	0.1272(4)	0.9227(2)	0.0825(14)
O5	0.3194(4)	0.3535(4)	0.5473(2)	0.0879(15)
C8	0.5947(4)	0.8604(5)	0.6670(3)	0.0448(14)
C7	0.5306(4)	0.8235(5)	0.5978(3)	0.0427(14)
C6	0.4718(4)	0.6937(5)	0.5910(3)	0.0463(14)
C13	0.9026(4)	0.8664(6)	0.8284(3)	0.0422(13)
C18	0.8501(5)	0.1234(6)	0.8592(3)	0.0526(15)
C12	0.8887(4)	0.7683(6)	0.7677(3)	0.0536(15)
C9	0.5983(4)	0.7688(6)	0.7295(3)	0.0528(15)
C15	0.0247(5)	0.6997(6)	0.9040(3)	0.0540(15)
C14	0.9713(4)	0.8344(6)	0.8964(3)	0.0515(15)
C5	0.3731(5)	0.7221(6)	0.4558(3)	0.0563(16)
C2	0.2670(5)	0.2440(6)	0.5263(3)	0.0587(17)

	x/a	y/b	z/c	U(eq)
C16	0.9438(5)	0.6350(6)	0.7774(3)	0.0593(17)
C11	0.4772(5)	0.5996(6)	0.6525(3)	0.0665(18)
C17	0.0116(5)	0.5992(6)	0.8437(4)	0.0679(18)
C10	0.5397(5)	0.6387(6)	0.7212(3)	0.0664(18)
C19	0.7849(5)	0.2534(5)	0.8253(3)	0.0727(19)
C4	0.2997(5)	0.6401(6)	0.3942(3)	0.081(2)
C3	0.2826(6)	0.1061(6)	0.5700(3)	0.078(2)
C1	0.1852(5)	0.2411(7)	0.4525(3)	0.091(2)

Table S10. Bond lengths (Å)

O2-C8	1.368(5)	**O2-H10**	0.82
O1-C5	1.220(6)	**N2-C18**	1.352(6)
N2-C13	1.417(6)	**N2-H4**	0.86
O4-C15	1.359(6)	**O4-H8**	0.82
N1-C5	1.352(6)	**N1-C6**	1.421(6)
N1-H15	0.86	**O3-C18**	1.223(6)
O5-C2	1.210(5)	**C8-C9**	1.379(6)
C8-C7	1.381(6)	**C7-C6**	1.378(6)
C7-H14	0.93	**C6-C11**	1.378(7)
C13-C14	1.380(7)	**C13-C12**	1.387(7)
C18-C19	1.497(6)	**C12-C16**	1.385(6)
C12-H5	0.93	**C9-C10**	1.380(6)
C9-H11	0.93	**C15-C14**	1.385(7)
C15-C17	1.394(7)	**C14-H9**	0.93
C5-C4	1.493(7)	**C2-C3**	1.473(7)
C2-C1	1.505(8)	**C16-C17**	1.358(7)
C16-H6	0.93	**C11-C10**	1.371(7)
C11-H13	0.93	**C17-H7**	0.93
C10-H12	0.93	**C19-H1**	0.96
C19-H3	0.96	**C19-H2**	0.96
C4-H16	0.96	**C4-H17**	0.96
C4-H18	0.96	**C3-H24**	0.96
C3-H22	0.96	**C3-H23**	0.96
C1-H19	0.96	**C1-H20**	0.96
C1-H21	0.96		

Table S11. Bond angles (°)

C8-O2-H10	109.5	**C18-N2-C13**	130.2(5)
C18-N2-H4	114.9	**C13-N2-H4**	114.9
C15-O4-H8	109.5	**C5-N1-C6**	129.4(4)
C5-N1-H15	115.3	**C6-N1-H15**	115.3
O2-C8-C9	118.1(5)	**O2-C8-C7**	121.8(5)
C9-C8-C7	120.1(5)	**C6-C7-C8**	119.8(5)
C6-C7-H14	120.1	**C8-C7-H14**	120.1
C7-C6-C11	120.6(5)	**C7-C6-N1**	123.4(5)
C11-C6-N1	116.1(5)	**C14-C13-C12**	121.2(5)
C14-C13-N2	122.6(5)	**C12-C13-N2**	116.2(5)
O3-C18-N2	121.1(5)	**O3-C18-C19**	122.1(5)
N2-C18-C19	116.8(5)	**C16-C12-C13**	118.4(5)
C16-C12-H5	120.8	**C13-C12-H5**	120.8
C8-C9-C10	119.2(5)	**C8-C9-H11**	120.4
C10-C9-H11	120.4	**O4-C15-C14**	121.6(5)
O4-C15-C17	117.4(5)	**C14-C15-C17**	121.1(5)
C13-C14-C15	118.6(5)	**C13-C14-H9**	120.7
C15-C14-H9	120.7	**O1-C5-N1**	122.9(5)
O1-C5-C4	121.8(5)	**N1-C5-C4**	115.4(5)
O5-C2-C3	121.9(5)	**O5-C2-C1**	121.3(6)
C3-C2-C1	116.8(5)	**C17-C16-C12**	122.1(5)
C17-C16-H6	119.0	**C12-C16-H6**	119.0
C10-C11-C6	119.0(5)	**C10-C11-H13**	120.5
C6-C11-H13	120.5	**C16-C17-C15**	118.6(6)
C16-C17-H7	120.7	**C15-C17-H7**	120.7
C11-C10-C9	121.3(5)	**C11-C10-H12**	119.3
C9-C10-H12	119.3	**C18-C19-H1**	109.5
C18-C19-H3	109.5	**H1-C19-H3**	109.5
C18-C19-H2	109.5	**H1-C19-H2**	109.5
H3-C19-H2	109.5	**C5-C4-H16**	109.5
C5-C4-H17	109.5	**H16-C4-H17**	109.5
C5-C4-H18	109.5	**H16-C4-H18**	109.5
H17-C4-H18	109.5	**C2-C3-H24**	109.5
C2-C3-H22	109.5	**H24-C3-H22**	109.5
C2-C3-H23	109.5	**H24-C3-H23**	109.5
H22-C3-H23	109.5	**C2-C1-H19**	109.5
C2-C1-H20	109.5	**H19-C1-H20**	109.5
C2-C1-H21	109.5	**H19-C1-H21**	109.5
H20-C1-H21	109.5		

Table S12. Anisotropic atomic displacement parameters ($Å^2$)

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U11 + ... + 2 h k a^* b^* U12]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O2	0.069(3)	0.045(2)	0.056(3)	0.0080(18)	-0.015(2)	-0.012(2)
O1	0.089(3)	0.052(2)	0.061(3)	0.018(2)	-0.016(2)	-0.023(2)
N2	0.052(3)	0.045(3)	0.040(3)	0.000(2)	-0.004(2)	-0.003(2)
O4	0.103(4)	0.064(3)	0.066(3)	-0.009(2)	-0.018(3)	0.031(3)
N1	0.074(4)	0.041(3)	0.053(3)	0.005(2)	-0.010(3)	-0.012(3)
O3	0.106(3)	0.066(3)	0.061(3)	-0.019(2)	-0.032(3)	0.022(3)
O5	0.111(4)	0.056(3)	0.091(3)	-0.006(2)	0.000(3)	-0.031(3)
C8	0.045(3)	0.038(3)	0.049(4)	0.002(3)	0.000(3)	0.001(3)
C7	0.049(4)	0.036(3)	0.040(3)	0.003(2)	-0.002(3)	-0.003(3)
C6	0.050(4)	0.043(3)	0.043(4)	0.001(3)	0.000(3)	-0.008(3)
C13	0.037(3)	0.047(3)	0.042(3)	0.002(3)	0.005(3)	-0.002(3)
C18	0.059(4)	0.048(3)	0.047(4)	0.004(3)	-0.004(3)	-0.005(3)
C12	0.055(4)	0.063(4)	0.042(4)	0.002(3)	0.005(3)	0.003(3)
C9	0.060(4)	0.056(4)	0.040(4)	0.008(3)	0.001(3)	-0.002(3)
C15	0.053(4)	0.060(4)	0.044(4)	0.002(3)	-0.005(3)	0.009(3)
C14	0.053(4)	0.053(4)	0.047(4)	-0.002(3)	0.002(3)	0.003(3)
C5	0.053(4)	0.050(4)	0.061(4)	0.003(3)	-0.005(3)	-0.001(3)
C2	0.065(4)	0.050(4)	0.060(4)	-0.012(3)	0.008(3)	-0.010(4)
C16	0.062(4)	0.071(4)	0.044(4)	-0.020(3)	0.006(3)	0.012(4)
C11	0.075(4)	0.063(4)	0.058(4)	0.012(3)	0.000(4)	-0.023(4)
C17	0.076(5)	0.054(4)	0.070(5)	-0.009(3)	0.002(4)	0.013(4)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C10	0.077(4)	0.070(4)	0.047(4)	0.021(3)	-0.006(3)	-0.013(4)
C19	0.088(5)	0.044(4)	0.079(5)	0.004(3)	-0.007(4)	0.007(3)
C4	0.090(5)	0.069(4)	0.074(5)	0.001(4)	-0.019(4)	-0.014(4)
C3	0.107(5)	0.061(4)	0.063(5)	-0.010(3)	0.007(4)	-0.006(4)
C1	0.091(5)	0.117(6)	0.061(5)	0.006(4)	-0.001(4)	-0.009(5)

Table S13. Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$)

	x/a	**y/b**	**z/c**	**U(eq)**
H10	0.6353	1.0420	0.6402	0.089
H4	0.7967	1.0048	0.7739	0.056
H8	1.1021	0.7314	0.9987	0.121
H15	0.3780	0.5600	0.5225	0.07
H14	0.5272	0.8861	0.5560	0.051
H5	0.8436	0.7914	0.7216	0.064
H11	0.6398	0.7944	0.7765	0.063
H9	0.9816	0.9018	0.9364	0.062
H6	0.9341	0.5679	0.7373	0.071
H13	0.4389	0.5108	0.6474	0.08
H7	1.0484	0.5095	0.8489	0.081
H12	0.5426	0.5763	0.7630	0.08
H1	0.7570	1.3065	0.8651	0.109
H3	0.7234	1.2210	0.7879	0.109
H2	0.8324	1.3161	0.8012	0.109
H16	0.2368	0.7000	0.3738	0.122
H17	0.2739	0.5518	0.4150	0.122
H18	0.3411	0.6159	0.3540	0.122
H24	0.3543	0.1067	0.6022	0.117
H22	0.2784	0.0249	0.5351	0.117
H23	0.2251	0.0968	0.6012	0.117
H19	0.1685	0.3397	0.4354	0.137
H20	0.1178	0.1932	0.4609	0.137
H21	0.2172	0.1887	0.4143	0.137